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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/825,751	04/03/2001	Corine A.M. Vernet	15966-750 CURA-250)	7299

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EXAMINER

YU, MISOOK

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 05/21/2003

18

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Applicant(s)

09/825,751

Applicant(s)

VERNET ET AL.

Examiner

MISOOK YU, Ph.D.

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 04 March 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 38, 41, 50-54 is/are pending in the application.
- 4a) Of the above claim(s) 50-54 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 38 and 41 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION*****Election/Restrictions***

Claims 1, 36, 38, 50-54 are pending and claims 50-54 drawn to method of making the instantly claimed product remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim because the product is not allowable. See claims rejection below. Claims 1-4, 38, and 41 are examined.

***Specification***

The disclosure **remains objected** to because it still contains the embedded hyperlink and/or other form of browser-executable still contains embedded hyperlink and/or other form of browser-executable code, see for example page 23. Applicant is requested to examine the entire specification very carefully. Applicant is required to delete **ALL** embedded hyperlinks and/or other form of browser-executable codes in the specification. See MPEP § 608.01.

***Claim Rejections - 35 USC § 112***

Claims 1-4, 38, and 41 remain rejected for recitation of "a mature form" under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant appears to argue that mature form of SEQ ID NO:20 is the polypeptide with first 22 amino acids being cleaved from SEQ ID NO:20. However, claim still say "a" mature form, not "the" mature form, which is still confusing about what is the reasonable property boundary claimed by the limitation for patent protection. All other rejections not repeated here are moot because the claims no longer recite the rejected limitation.

Claims 1-4, 38, and 41 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, **had poss ssion** of the claimed invention. Applicant argues that the claims are amended and variants are no longer recited. This argument is not

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persuasive because claims are still drawn to "a mature form" of SEQ ID NO:20. The specification teaches only one mature form but recitation of the indefinite article "a" in the claim suggests that the claims are drawn to more than one mature form. Therefore this rejection is maintained.

### ***Claim Rejections - 35 USC § 101***

Claims 1-4, 38, and 41 remain rejected for reason of record under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility.

Applicant argues that the claimed invention is useful in treatment of patients suffering from cancer and other cell proliferative disorders. This assertion is credible and specific, however the Office maintains the utility rejection because the disclosure including Dr. Patturajan's declaration along with the new attached expression data and the Table 21 at page 122 of the specification do not meet the substantial part of the three prong tests in the utility rejection. As stated before in the previous Office action, the specification does not show whether the claimed polypeptide is overexpressed or underexpressed in a specific, diseased tissue compared to the healthy tissue control. The expression data at Table 21 Dr. Patturajan mentioned in the declaration as well as the attached data in the declaration show the nucleic acid expression using cell lines. It is the Office's position that cell line expression could not be extrapolated to *in vivo* expression because it is well known in the art that characteristics of cultured cell lines generally differ significantly from the characteristics of *in vivo* primary cancers or metastatic cancers. Freshney (Culture of Animal Cells, A Manual of Basic Technique, Alan R. Liss, Inc., 1983, New York, page 4) teaches that it is recognized in the art that there are many differences between cultured cells and their counterparts *in vivo*. These differences stem from the dissociation of cells from a three-dimensional geometry and their propagation on a two-dimensional substrate. Specific cell interactions characteristic of histology of the tissue are lost. The culture environment lacks the input of the nervous and endocrine systems involved in homeostatic regulation *in vivo*.

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Without this control, cellular metabolism may be more constant *in vitro* but may not be truly representative of the tissue from which the cells were derived. This has often led to tissue culture being regarded in a rather skeptical light (p. 4, see Major Differences *In Vitro*). Further, Dermer (Bio/Technology, 1994, 12:320) teaches that, "petri dish cancer" is a poor representation of malignancy, with characteristics profoundly different from the human disease. Further, Dermer teaches that when a normal or malignant body cell adapts to immortal life in culture, it takes an evolutionary -type step that enables the new line to thrive in its artificial environment. This step transforms a cell from one that is stable and differentiated to one that is not, yet normal or malignant cells *in vivo* are not like that. The reference states that evidence of the contradictions between life on the bottom of a lab dish and in the body has been in the scientific literature for more than 30 years. Clearly it is well known in the art that cells in culture exhibit characteristics different from those *in vivo* and cannot duplicate the complex conditions of the *in vivo* environment involved in host-tumor and cell-cell interactions. Thus, based on the cell culture data presented in the specification, it could not be predicted that either SEQ ID NO:20 or nucleic acid encoding SEQ ID NO:20 is expressed *in vivo*.

Further, it is also the Office's position that mRNA expression data could not be extrapolated protein expression data because the art recognizes that expression of mRNA does not dictate nor predict the translation of such mRNA into a polypeptide. For example, Alberts et al. (Molecular Biology of the Cell, 3rd edition, 1994, page 465) teach that translation of ferritin mRNA into ferritin polypeptide is blocked during periods of iron starvation. Likewise, if excess iron is available, the transferrin receptor mRNA is degraded and no transferrin receptor polypeptide is translated. Many other proteins are regulated at the translational level rather than the transcriptional level. For instance, Shantz and Pegg (Int J of Biochem and Cell Biol., 1999, Vol. 31, pp. 107-122) teach that ornithine decarboxylase is highly regulated in the cell at the level of translation and that translation of ornithine decarboxylase mRNA is dependent on the secondary structure of the mRNA and the availability of eIF-4E, which mediates translation initiation. McClean and Hill (Eur J of Cancer, 1993, vol. 29A, pp. 2243-2248) teach that p-glycoprotein can be overexpressed in CHO cells following exposure to radiation, without

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any concomitant overexpression of the p-glycoprotein mRNA. In addition, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Thus, predictability of protein translation is not solely contingent on mRNA expression due to the multitude of homeostatic factors affecting transcription and translation.

Therefore, it is concluded that the specification, applicant's argument, or Dr. Patturajan's declaration does not teach a substantial use of the claimed invention. Applicant is invited to present data showing the claimed polypeptide is overexpressed or underexpressed in a specific, diseased tissue compared to the healthy tissue control in order to overcome this rejection if expression is the main substantial utility of the claimed invention.

New references are provided to applicants but these references are used to make a point why the rejection is being maintained in spite of applicant's argument and Dr. Patturajan's declaration along with the new attached data expression data.

### ***35 U.S.C. § 112, First Paragraph***

Claims 1-4, 36, and 39 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know ***how to use*** the claimed invention.

### ***Claim Rejections - 35 USC § 102***

Rejection of claims 1-4, 38, and 41 under 35 U.S.C. 102(b) as being anticipated by either Chang et al (IDS C15, 1994, J. Biol. Chem. Vol. 269, pages 28227-28234) or US Pat. 5,658,882 (8-19-1997) **is withdrawn** because the prior no longer anticipates the amended claims.

### ***Conclusion***

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**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu

May 15, 2003

  
**MARY E. MOSHER**  
**PRIMARY EXAMINER**  
**GROUP 1800-7600**